Evaluate Vantage

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RSVVW 2021 – Pfizer gets maternal

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Positive phase 2 data with the group's maternal RSV vaccine set up a busy 2022 for work on the infectious disease.

Pfizer had already surprised investors with positive findings in adults with its respiratory syncytial virus (RSV) vaccine RSVpreF. Now promising mid-stage data suggest that RSVpreF could also have a role in the maternal setting.

Here, vaccines are given to pregnant women to protect their infants from RSV once they are born. An abstract for the upcoming RSVVW conference showed that, in a phase 2b trial, RSVpreF had 85% efficacy in preventing infant lower respiratory tract infections. This looks slightly better than efficacy seen with Astrazeneca and Sanofi's long-acting antibody nirsevimab. However, competition in RSV is fierce, with several pivotal readouts set for next year.

The latest data could bode well for Pfizer's own pivotal trials. Its maternal protection study of RSVpreF is due an interim analysis in mid-2022, while the Renoir trial in adults aged 60 or over is expected to read out in the first quarter.

Pfizer vs Glaxo

This puts Pfizer on a collision course with Glaxosmithkline; the latter recently brought forward the readout of a pivotal trial of its adult RSV vaccine to the first half of next year, thanks to faster-than-expected enrolment.

The UK group has a separate maternal vaccine candidate, RSVPreF3, with data from the pivotal Grace trial due in the second half of 2022. The prospects of this project also got a boost with the abstract drop from the RSVVW meeting: immunogenicity data from a phase 2 trial showed that RSV-A/B neutralising antibody levels in vaccinated women increased more than tenfold at day 31 post-jab.

In the infants of vaccinated women, neutralising antibody levels were higher than those seen in infants whose mothers received placebo, an effect that persisted for six months.

Efficacy data for RSVPreF3 were not detailed in the abstract, but Leerink analysts noted that Novavax's failed RSV project Resvax only showed two to threefold increases in neutralising antibodies in its pivotal trial, Prepare.

Pfizer and Glaxo now need all of this to translate into an efficacy signal in phase 3 – not an easy task in RSV, a field that has been marked by blow-ups. Indeed, only one product, Abbvie and Sobi's fusion antibody Synagis, has been approved in 22 years.

However, this product, which is given shortly after birth to provide protection against RSV, is far from perfect: it is only indicated for high-risk infants, and has a steep $6,000 price tag and a complex treatment regimen involving five monthly doses.

Nirsevimab first?

Still, Astra and Sanofi's nirsevimab is set to beat the vaccines to market, with filings due in Europe in the first quarter of next year, and in the US in the second half. This is essentially designed as a better version of Synagis, with its longer half-life meaning a single dose can provide protection over a full RSV season.

Nirsevimab's developers hope that it could be used in all infants, regardless of their risk of RSV. The companies already reported data from healthy late pre-term and term infants from the Melody trial at IDWeek; that study met its primary endpoint, with nirsevimab reducing the rate of medically attended RSV lower respiratory tract infections by 75% versus placebo.

Meanwhile, the first efficacy data in high-risk infants, from the Medley study, will feature at the RSVVW meeting. That trial compares nirsevimab versus Synagis in high-risk children, namely premature infants and those with chronic lung and congenital heart diseases.

Safety was the primary endpoint, and nirsevimab showed a similar adverse event rate to Synagis. The abstract also disclosed seven cases of medically attended RSV lower respiratory tract infections, with an event rate of 0.6% in the nirsevimab and 1% in the Synagis arm. Leerink calculated that this equated to four events with nirsevimab and three with Synagis, giving a relative risk reduction of 33% with the former.

The analysts conceded that the event counts were small, but said the data suggested that nirsevimab was at least as effective as Synagis in high-risk infants. They expect nirsevimab to become standard of care, replacing Synagis in preterm infants.

However, Pfizer's latest data suggest that vaccines could provide stiff competition to Astra and Sanofi's antibody, with the usual caveats about cross-trial comparisons.

If both approaches do make it to market, each has its pros and cons. Timing maternal vaccination can be tricky to ensure protection of the infant during the RSV season, whereas antibodies can be targeted more accurately to the times of year when the virus is most prevalent. Maternal vaccines, however, could be cheaper.

Leerink had previously expected antibodies to capture around two thirds of the $3bn infant RSV prophylaxis market, and vaccines around a third. However, they added that this estimate could change if efficacy with the vaccines held up in phase 3 – a big ask, but now not as impossible as it once seemed.

Selected RSV projects in clinical development				
Product	**Company**	**Description**	**2026e sales ($m)**	**Trial details**
Marketed				
Synagis	Abbvie/Sobi	Fusion antibody	666	Indicated for prevention of RSV infections in high-risk infants
Phase 3				
Nirsevimab (SP0232)	Sanofi/Astrazeneca	Fusion antibody	586	Melody in healthy infants reported; Medley in high-risk infants, initial data at RSVVW 2021; filings planned 2022
GSK3844766A	Glaxosmithkline	Protein subunit vaccine, adjuvanted	1,037	Aresvi 004 in adults ≥60, data due H1 2022 (from H2 2022)
RSVPreF3 (GSK3888550A)	Glaxosmithkline	Protein subunit vaccine, unadjuvanted	108	Grace maternal protection trial, data due H2 2022
RSVpreF (PF-06928316)	Pfizer	Protein subunit vaccine	222	Renoir in adults ≥60, data due Q1 2022; Maternal protection trial, interim analysis due mid-2022
Ad26.RSV.preF	Johnson & Johnson	Adenovirus type 26 viral vector vaccine	16	Evergreen in adults ≥60, data due H2 2022*
Clesrovimab (MK-1654)	Merck & Co	Fusion antibody	10	MK-1654-007 in high-risk infants; ph2/3 MK-1654-004 in healthy infants, data due 2022*
Rilematovir (JNJ-53718678)	Johnson & Johnson	Oral RSV F-protein fusion inhibitor	–	Daisy in hospitalised children; Primrose in adult outpatients
Phase 2				
MVA-BN RSV	Bavarian Nordic	Vaccinia virus Ankara vector vaccine	–	Human challenge trial data reported Sep 2021; ph3 in elderly planned for 2022
Phase 1				
mRNA-1345	Moderna	mRNA vaccine	–	Healthy volunteer trial, 5mth immunogenicity data at RSVVW 2021; ph2/3 in adults expected to begin YE 2021
**Leerink estimate. Source: Evaluate Pharma & clinicaltrials.gov.*				

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